## SUPPORT FOR THE AMENDMENTS

The specification has been amended to recite a claim of priority to related International and Japanese patent applications, as set forth in the originally filed Application Data Sheet. In addition, a substitute abstract is provided to address the Examiner's objection to the original abstract. Support for these amendments is found in the application as originally filed.

The present amendment amends claims 1-6, 8 and 12-17, and adds new claims 18-20.

Claims 1-6, 8 and 12-17 have been amended, and new claims 18-20 have been added, to place these claims in a better condition for allowance. Support for these amendments is provided by the originally filed claims and specification.

Support for newly added claims 18 and 19 is found at specification page 13, lines 4-10, as well as original claim 2.

Support for newly added claim 20 is found at specification page 8, lines 20-23, page 19, lines 24-28, and page 20, lines 1-11.

It is believed that these amendments have not resulted in the introduction of new matter.

## REMARKS

Claims 1-20 are currently pending in the present application. Claims 1-6, 8 and 12-17 have been amended, and new claims 18-20 have been added, by the present amendment. Claims 9 and 16 stand withdrawn from consideration by the Examiner as being directed to a non-elected invention.

The rejection of claims 1-8, 10-15 and 17 under 35 U.S.C. § 103(a) as being obvious over Bosch (U.S. Patent 5,510,118) in view of Yamakawa (Journal of Controlled Release) is respectfully traversed, with respect to claims 1-20.

Amended claim 1 is directed to a process for producing a fine dispersion of a poorly soluble drug, wherein the process comprises: suspending the poorly soluble drug in a liquid *containing no deflocculant* to obtain a suspension; introducing the suspension into a *high-pressure homogenizer* to subject the suspension to a high-pressure treatment to obtain a dispersion; and *adding a deflocculant* to the dispersion to deagglomerate aggregated particles contained therein.

Bosch describes a process for preparing a drug having a solubility in water of less than about 10 mg/mL and an average particle diameter of less than about 400 nm, wherein the process comprises: preparing a premix of the drug and a surface modifier; transferring the premix to a microfluidizer having an interaction chamber capable of producing shear, impact, cavitation and attrition forces; and subjecting the premix to shear, impact, cavitation and attrition forces to reduce the particle size of the drug (See e.g., abstract, column 3, lines 65-67, column 4, lines 1-10 and 56-61, claim 1). Bosch describes that it is preferred, but not essential, that the surface modifier be present in the premix (See e.g., column 7, lines 55-56). Bosch describes that if the surface modifier was not present in the premix, then the surface modifier must be added to the dispersion after attrition (See e.g., column 8, lines 16-18).

Yamakawa describes that 1-cyclopropyl-8-methyl-7-[5-methyl-6-(methylamino)-3-pyridinyl]-4-oxo-1,4-dihydro-3-quinolinecarboxylic acid (a.k.a., "T-3912") has an intrinsic solubility in water at a physiological pH of 7 of approximately 2 $\mu$g/mL (See e.g., abstract). Yamakawa describes that a stable aqueous liquid formulation of T-3912 can be obtained with the combined use of $Mg^{2+}$ ions, hydroxypropyl-$\beta$-cyclodextrin (HP$\beta$CD) and polyvinylpyrrolidone (PVP) (See e.g., abstract).

As discussed in the present specification and shown by the comparative experimental data provided therein, Applicants have discovered that the inventive fine dispersions of a poorly soluble drug of Examples 1-15, which were produced by the process of the present invention comprising suspending the poorly soluble drug in a liquid containing no deflocculant to obtain a suspension, introducing the suspension into a high-pressure homogenizer to subject the suspension to a high-pressure treatment to obtain a dispersion, and subsequently adding a deflocculant to the dispersion to deagglomerate aggregated particles contained therein, exhibited superior properties with respect to a narrow particle size distribution and an improved dispersion stability (See e.g., Examples 1-15, Tables 1-8, Figs. 1-7).

Unlike the inventive fine dispersions of a poorly soluble drug produced by the process of the present invention, the traditional fine dispersions of a poorly soluble drug of Comparative Examples 1-9, which were produced by a conventional process similar to that described in Bosch comprising suspending the poorly soluble drug in a liquid containing deflocculant to obtain a suspension, and introducing the suspension into a high-pressure homogenizer (e.g., a microfluidizer) to subject the suspension to a high-pressure treatment to obtain a dispersion, exhibited inferior properties with respect to an undesirably wide particle size distribution and a reduced dispersion stability (See e.g., Comparative Examples 1-9, Tables 1, 2, 5, 6 and 8, Figs. 1-7).

Unlike the process of the present invention, Bosch describes that the surface modifier is preferably present before microfluidization (See e.g., column 7, lines 55-56). Bosch mentions that if the surface modifier was not added before microfluidization, then the surface modifier must be added thereafter (See e.g., column 8, lines 16-18).

Based on the disclosure of Bosch, a skilled artisan would reasonably expect that fine dispersions of a poorly soluble drug would exhibit either slightly improved properties if the surface modifier is added before microfluidization in accordance with the preferred embodiment described therein, or similar properties regardless of whether the surface modifier is added before or after microfluidization.

Contrary to the disclosure of Bosch however, Applicants have discovered that fine dispersions of a poorly soluble drug exhibit superior properties with respect to a narrow particle size distribution and an improved dispersion stability when produced by the process of present invention, which comprises suspending the poorly soluble drug in a liquid containing no deflocculant to obtain a suspension, introducing the suspension into a high-pressure homogenizer to subject the suspension to a high-pressure treatment to obtain a dispersion, and adding a deflocculant to the dispersion to deagglomerate aggregated particles contained therein, as presently claimed.

Bosch and Yamakawa, when considered alone or in combination, fail to recognize that fine dispersions of a poorly soluble drug exhibit superior properties with respect to a narrow particle size distribution and an improved dispersion stability when produced by a process comprising suspending the poorly soluble drug in a liquid containing no deflocculant to obtain a suspension, introducing the suspension into a high-pressure homogenizer to subject the suspension to a high-pressure treatment to obtain a dispersion, and adding a deflocculant to the dispersion to deagglomerate aggregated particles contained therein, as presently claimed.

Withdrawal of this ground of rejection is respectfully requested.

The objection to the abstract is obviated by the attached rewritten abstract. Withdrawal of this ground of objection is respectfully requested.

In conclusion, Applicants submit that the present application is now in condition for allowance and notification to this effect is earnestly solicited.

Respectfully submitted,

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